



# UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE  
United States Patent and Trademark Office  
Address: COMMISSIONER FOR PATENTS  
P.O. Box 1450  
Alexandria, Virginia 22313-1450  
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
-----------------	-------------	----------------------	---------------------	------------------

10/763,681

01/23/2004

Salvatore Atzeni

ATZENI-NP

7482

21710 7590 06/08/2007  
BROWN, RUDNICK, BERLACK & ISRAELS, LLP.  
BOX IP, 18TH FLOOR  
ONE FINANCIAL CENTER  
BOSTON, MA 02111

EXAMINER

LIVEDALEN, BRIAN J

ART UNIT

PAPER NUMBER

2878

MAIL DATE

DELIVERY MODE

06/08/2007

PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

## Office Action Summary

Application No.

10/763,681

Applicant(s)

ATZENI ET AL.

Examiner

Brian J. Livedalen

Art Unit

2878

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 13 February 2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-29 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-14, 16-24 and 27-29 is/are rejected.
- 7) ☒ Claim(s) 15, 25, and 26 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 08 July 2004 is/are: a) ☐ accepted or b) ☒ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- ☒ Notice of References Cited (PTO-892)
- ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- ☐ Information Disclosure Statement(s) (PTO/SB/08)  
Paper No(s)/Mail Date \_\_\_\_\_
- ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date \_\_\_\_\_
- ☐ Notice of Informal Patent Application
- ☐ Other: \_\_\_\_\_

## **DETAILED ACTION**

### ***Drawings***

New corrected drawings in compliance with 37 CFR 1.121(d) are required in this application because text and reference numbers are handwritten. Applicant is advised to employ the services of a competent patent draftsman outside the Office, as the U.S. Patent and Trademark Office no longer prepares new drawings. The corrected drawings are required in reply to the Office action to avoid abandonment of the application. The requirement for corrected drawings will not be held in abeyance.

### ***Claim Objections***

Claim 1 recites the limitation "said low-frequency reference modulation products." There is insufficient antecedent basis for this limitation in the claim.

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-7, 9, 10, 12, 13, 14, 16-18, 20-24, and 27-29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Berndt et al. (5196709) in view of Wolleschensky et al. (2003/0067607).

In regard to claims 1, 16, and 20, Berndt discloses (fig. 1) a method of spectrographic measurement, including generating light energy using an excitation source (3), the light energy being cause to fall on a sample (4) to be assayed, causing the sample to output an output optical signal; generating a plurality of modulation frequencies (5a); generating a plurality of heterodyne frequencies, each of the heterodyne frequencies being associated with one of the modulation frequencies; generating a plurality of heterodyne frequencies to form a set of heterodyne signals at the heterodyne frequencies, each of the heterodyne frequencies being associated with one of the modulation frequencies; coupling the modulation frequencies to the excitation source, causing the excitation source to generate excitation energy modulated in intensity in proportion to the modulation frequencies (column 9, lines 14-34); sampling a portion of the excitation energy to form a reference excitation signal (column 10, lines 7-31); intensifying (6) an image to form an intensified image modulated with the plurality of modulation frequencies; receiving the intensified image modulated with the plurality of modulation frequencies on a multielement optical detector (6); generating a plurality of measurement signals using the multielement detector, each measurement signal associated with a single one of the elements; for each measurement signal associated with a single one of the elements of the multielement optical detector (column 9, lines 35-58), mixing (9) the measurement signal with the heterodyne signal to generate a

plurality of low-frequency measurement modulation products; one low-frequency modulation product being associated with each of the modulation frequencies and having the difference between a single modulation frequency and its associated heterodyne frequency having a measurement amplitude and phase; mixing (7) the reference excitation energy with the heterodyne signal to generate a plurality of reference modulation products; one reference modulation product being associated with each of the modulation frequencies and having the difference between a single modulation frequency and its associated heterodyne frequency having a reference amplitude and phase; each of the reference modulation products being associated with one of the low-frequency measurement modulation products; and for each of the plurality of low-frequency measurement modulation products, comparing, using a calculation device (8), the low-frequency measurement modulation product to its associated low-frequency measurement modulation product to its associated reference modulation product to generate an output signal indicating characteristics of the sample at the region on the sample associated with each of the elements (column 9, line 59 – column 10, line 14). Berndt remains silent regarding focusing the output signal as an image modulated with the plurality of modulated frequencies on an image intensifier. However, Wolleschensky discloses (fig. 5) a similar spectrographic measurement system that includes focusing optics (AO) to focus an output signal as an image modulated with the plurality of modulated frequencies on an image intensifier (page 3, paragraph 0044). It would have been obvious to one of ordinary skill in the art at the

Art Unit: 2878

time the invention was made to include imaging optics as taught by Wolleschensky in order to properly image the output signal emitted by the sample.

In regard to claim 17, Berndt discloses (fig. 1) an apparatus for performing fluorescence measurement, including a light source (3) generating laser excitation energy, oriented to illuminate a sample (4) to be measured and cause the sample to emit fluorescent energy; a frequency generator (5a) generating a plurality of modulation frequencies and heterodyne frequencies, each of the heterodyne frequencies being associated with one of the modulation frequencies; generating a plurality of heterodyne frequencies to form a set of heterodyne signals at the heterodyne frequencies, each of the heterodyne frequencies being associated with one of the modulation frequencies; the frequency generator being coupled to the excitation source, causing the excitation source to generate excitation energy modulated in intensity in proportion to the modulation frequencies (column 9, lines 14-34); sampling a portion of the excitation energy to form a reference excitation signal (column 10, lines 7-31); an image intensifier (6) positioned to receive an image to form an intensified image modulated with the plurality of modulation frequencies; a multielement optical detector (6) for receiving the intensified image modulated with the plurality of modulation frequencies and generating a plurality of measurement signals using the multielement detector, each measurement signal associated with a single one of the elements; for each measurement signal associated with a single one of the elements of the multielement optical detector (column 9, lines 35-58), a mixer (9) to mix the measurement signal with the heterodyne signal to generate a plurality of low-frequency measurement modulation products; one

low-frequency modulation product being associated with each of the modulation frequencies and having the difference between a single modulation frequency and its associated heterodyne frequency having a measurement amplitude and phase; a mixer (7) to mix the reference excitation energy with the heterodyne signal to generate a plurality of reference modulation products; one reference modulation product being associated with each of the modulation frequencies and having the difference between a single modulation frequency and its associated heterodyne frequency having a reference amplitude and phase; each of the reference modulation products being associated with one of the low-frequency measurement modulation products; and for each of the plurality of low-frequency measurement modulation products, each of the low-frequency measurement modulation products and their associated low-frequency reference modulation products indicating phase and modulation information (column 9, line 59 – column 10, line 14). Berndt remains silent regarding an optical member for diverting a portion of the laser. However, Wolleschensky discloses (fig. 5) a similar spectrographic measurement system that includes an optical member (BS1) to divert a portion of the laser to generate a reference signal (page 3, paragraph 0041). It would have been obvious to one of ordinary skill in the art at the time the invention was made to include an optical member as taught by Wolleschensky in order to efficiently and inexpensively separate a reference and measurement beam. Berndt remains silent regarding focusing the output signal as an image modulated with the plurality of modulated frequencies on an image intensifier. However, Wolleschensky further discloses (fig. 5) a similar spectrographic measurement system that includes focusing

optics (AO) to focus an output signal as an image modulated with the plurality of modulated frequencies on an image intensifier (page 3, paragraph 0044). It would have been obvious to one of ordinary skill in the art at the time the invention was made to include imaging optics as taught by Wolleschensky in order to properly image the output signal emitted by the sample.

In regard to claim 24, Berndt discloses (fig. 1) a method of spectrographic measurement, including generating light energy using an excitation source (3), the light energy being cause to fall on a sample (4) to be assayed, causing the sample to output an output optical signal; generating a plurality of modulation frequencies (5a); generating a plurality of heterodyne frequencies, each of the heterodyne frequencies being associated with one of the modulation frequencies; generating a plurality of heterodyne frequencies to form a set of heterodyne signals at the heterodyne frequencies, each of the heterodyne frequencies being associated with one of the modulation frequencies; coupling the modulation frequencies to the excitation source, causing the excitation source to generate excitation energy modulated in intensity in proportion to the modulation frequencies (column 9, lines 14-34); sampling a portion of the excitation energy to form a reference excitation signal (column 10, lines 7-31); intensifying (6) an image to form an intensified image modulated with the plurality of modulation frequencies; receiving the intensified image modulated with the plurality of modulation frequencies on a multielement optical detector (6); generating a plurality of measurement signals using the multielement detector, each measurement signal



associated with a single one of the elements; for each measurement signal associated with a single one of the elements of the multielement optical detector (column 9, lines 35-58), mixing (9) the measurement signal with the heterodyne signal to generate a plurality of low-frequency measurement modulation products; one low-frequency modulation product being associated with each of the modulation frequencies and having the difference between a single modulation frequency and its associated heterodyne frequency having a measurement amplitude and phase; mixing (7) the reference excitation energy with the heterodyne signal to generate a plurality of reference modulation products; one reference modulation product being associated with each of the modulation frequencies and having the difference between a single modulation frequency and its associated heterodyne frequency having a reference amplitude and phase; each of the reference modulation products being associated with one of the low-frequency measurement modulation products; and for each of the plurality of low-frequency measurement modulation products, comparing (8) the low-frequency measurement modulation product to its associated low-frequency measurement modulation product to its associated reference modulation product to generate an output signal indicating characteristics of the sample at the region on the sample associated with each of the elements (column 9, line 59 – column 10, line 14); for each element, fitting the modulation data points to a first curve using a mathematical fitting technique; for each element fitting the phase data points to a second curve using a mathematical fitting technique; comparing the first and second curves to a database to determine characteristics of the sample; and displaying the characteristics (column 12,

line 48 – column 13, line 20). Berndt remains silent regarding focusing the output signal as an image modulated with the plurality of modulated frequencies on an image intensifier. However, Wolleschensky discloses (fig. 5) a similar spectrographic measurement system that includes focusing optics (PO) to focus an output signal as an image modulated with the plurality of modulated frequencies on an image intensifier (page 3, paragraph 0044). It would have been obvious to one of ordinary skill in the art at the time the invention was made to include imaging optics as taught by Wolleschensky in order to properly image the output signal emitted by the sample.

In regard to claim 27, Berndt discloses (fig. 1) a method of spectrographic analysis including generating light (3) modulated by a plurality of modulation frequencies (5a); generating (5b) a plurality of heterodyne frequencies each associated with one of the modulation frequencies, each of the heterodyne frequencies being different from its corresponding modulation frequency (column 9, lines 14-34); causing the measurement light to fall on a sample (4) to be assayed and stimulate the production of a measurement light signal; sending the measurement light signal and the heterodyne frequencies to a first mixer (9); sending the heterodyne frequencies and a reference light to a second mixer (7); and sending the output of the first and second mixers for analysis of the sample (column 9, lines 35-58, column 10, lines 7-31, column 9, line 59 – column 10, line 14). Berndt remains silent regarding splitting the light. However, Wolleschensky discloses (fig. 5) a similar spectrographic measurement system that includes an optical member (BS1) to divert a portion of the laser to generate

Art Unit: 2878

a reference signal (page 3, paragraph 0041). It would have been obvious to one of ordinary skill in the art at the time the invention was made to include an optical member as taught by Wolleschensky in order to efficiently and inexpensively separate a reference and measurement beam. Berndt fails to disclose the calculation device being a computer. However, Wolleschensky discloses using a computer to extract phase and modulation information (page 4, paragraph 0054). It would have been obvious to one of ordinary skill in the art at the time the invention was made to use a computer as taught by Wolleschensky in order to digitally perform calculations.

In regard to claim 2, Berndt discloses that the output signal is numerically processed to generate changes over time (column 9, lines 14-34).

In regard to claim 3, Berndt discloses that the output signal may be graphically displayed (column 12, line 48 – column 13, line 20).

In regard to claim 4, Berndt discloses is numerically processed to generate a desired parameter (column 12, line 48 – column 13, line 20).

In regard to claim 5, Berndt discloses that the excitation source is a laser (column 9, lines 14-34).

In regard to claim 6, Berndt discloses that the output optical signal includes fluorescent energy from the sample (abstract).

In regard to claim 7, Berndt discloses that the modulation frequencies are harmonically related (column 9, lines 14-34).

In regard to claim 9, Berndt discloses that the excitation source is a pulsed laser (column 9, lines 14-34).

In regard to claim 10, Berndt discloses that the excitation source is a pulsed-dye laser (column 3, lines 8-15).

In regard to claim 12, Berndt discloses that the reference modulation products are the low-frequency reference modulation products output during the mixing operation (column 9, line 59 – column 10, line 14):

In regard to claim 13, Berndt discloses that the comparison is done by measuring the relative phase and amplitude of the low-frequency measurement modulation product as compared to the reference modulation product and generating a modulation data point and a phase data point (column 9, line 59 – column 10, line 14).

In regard to claim 14, Berndt discloses for each element, fitting the modulation data points to a first curve using a mathematical fitting technique; for each element fitting the phase data points to a second curve using a mathematical fitting technique; comparing the first and second curves to a database to determine characteristics of the sample; and displaying the characteristics (column 12, line 48 – column 13, line 20).

In regard to claim 18, Berndt in view of Wolleschensky discloses in Wolleschensky, that the optical member is a partially silvered mirror (page 3, paragraph 0041).

In regard to claim 21, Berndt in view of Wolleschensky discloses an apparatus for detecting for fluorescence detection with a calculation device (8) as set forth above. Berndt fails to disclose the calculation device being a computer. However, Wolleschensky discloses using a computer to extract phase and modulation information (page 4, paragraph 0054). It would have been obvious to one of ordinary skill in the art

Art Unit: 2878

at the time the invention was made to use a computer as taught by Wolleschensky in order to digitally perform calculations.

In regard to claims 22 and 23, Berndt in view of Wolleschensky discloses in Wolleschensky, that the optics are microscope confocal optics (page 3, paragraph 0044).

In regard to claims 28 and 29, Berndt discloses that the heterodyne frequencies are derived from and synchronized with the modulation frequencies (column 9, lines 14-34).

Claim 8 is rejected under 35 U.S.C. 103(a) as being unpatentable over Berndt et al. (5196709) in view of Wolleschensky et al. (2003/0067607) as applied to claim 1, and in further view of Drain (4180328).

In regard to claim 8, Berndt in view of Wolleschensky discloses an excitation source as set forth above but fails to disclose the excitation source being modulated by a Pockel's cell. However, Drain discloses a similar system that uses an excitation source modulated by a Pockel's cell (column 1, lines 49-51). It would have been obvious to one of ordinary skill in the art at the time the invention was made to use Pockel's cell as taught by Drain in order to inexpensively provide a pulsed light source.

Claim 11 is rejected under 35 U.S.C. 103(a) as being unpatentable over Berndt et al. (5196709) in view of Wolleschensky et al. (2003/0067607) as applied to claim 1, and in further view of Cruce et al. (5981957).

In regard to claim 11, Berndt in view of Wolleschensky discloses an excitation source as set forth above but fails to disclose the excitation source being a light emitting diode. However, Cruce discloses a similar system that uses a light emitting diode as an excitation source (column 6, lines 57-64). It would have been obvious to one of ordinary skill in the art at the time the invention was made to use a light emitting diode as taught by Cruce in order to inexpensively provide a pulsed light source.

Claim 19 is rejected under 35 U.S.C. 103(a) as being unpatentable over Berndt et al. (5196709) in view of Wolleschensky et al. (2003/0067607) as applied to claim 17, and in further view of Hill (2003/0043384).

In regard to claim 19, Berndt in view of Wolleschensky discloses an optical member as set forth above but fails to disclose the optical member being a prism. However, Hill discloses (fig. 1A) a similar system, which uses a prism (240) to separate a reference beam and a measurement beam (page 5, paragraph 0054). It would have been obvious to one of ordinary skill in the art at the time the invention was made to use a prism as taught by Hill in order to configure the system as desired.

***Allowable Subject Matter***

Claims 15, 25, and 26 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Art Unit: 2878

The following is a statement of reasons for the indication of allowable subject matter: Claims 15, 25, and 26 are neither anticipated nor made obvious by the prior art of record.

In regard to claims 15, 25, and 26, the prior art fails to disclose a method as set forth in combination with the method of before excitation energy falls on the sample, the system is calibrated by first using a standard consisting of a zero lifetime scattering solution.

### ***Conclusion***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian J. Livedalen whose telephone number is (571) 272-2715. The examiner can normally be reached on 7:30 am to 4:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Georgia Epps can be reached on (571) 272-2328. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Art Unit: 2878

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

bjl



THANH X. LUU  
PRIMARY EXAMINER